

CLAIM LISTING:

The following listing of claims replaces all prior listings of claims in this application.

1. ***(Currently Amended)*** A method for determining whether an agent can be used to reduce the proliferation, inhibit the growth, and/or cause the death of lung cancer cells or inhibit the growth of a cancer cell population, comprising the steps of: a) obtaining a sample of lung cancer cells; b) determining and quantifying the level of expression of a marker gene in the said lung cancer cells of marker genes, wherein said marker gene is comprising ABCC5, GTF2H2 and/or ERCC2; and c) identifying that an said agent can be used to reduce the proliferation, inhibit the growth, and/or cause the death of said lung cancer cells when at least one expression of said markers gene is expressed at a certain level comparable to a previously determined level of said marker gene in cells with known sensitivity to said agent.

2. ***(Currently Amended)*** The method of claim 1, wherein the said level of expression of said marker genes in the said sample is assessed by detecting the presence in the said sample of a transcribed polynucleotide or portion thereof, wherein the transcribed polynucleotide comprises said two or more of said markers gene.

3. ***(Currently Amended)*** The method of claim 2, wherein the said transcribed polynucleotide is an mRNA or miRNA.

4. ***(Currently Amended)*** AThe method of claim 2, wherein the said transcribed polynucleotide is a cDNA.

5. ***(Withdrawn)*** The method of claim 1, wherein the level of expression of said marker genes comprising ABCC5, GTF2H2 and ERCC2 in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to said marker genes.

6. ***(Currently Amended)*** The method of claim 2, wherein the step of detecting further comprises amplifying the said transcribed polynucleotide using RT-PCR.

7. **(Currently Amended)** The method of claim 6~~1~~, wherein ~~the step of detecting the level of expression includes:~~
initially screening a plurality of genes representing different functional classes;
evaluating an expanded group of genes represented by genes that are positively or negatively associated in the initial screening;
comparing the expression of the positively and negatively associated genes said level of expression of said marker gene is used with the level of expression of another marker gene to form at least one interactive gene expression index (IGEI), wherein said IGEI comprises a ratio of said level of expression of said marker gene and said level of expression of another marker gene
using individual gene analysis and IGEI analysis, and
developing at least one model of the level that describes an association between the level of detection of the expression of at least one of the markers identified in Tables 1 and 5 and reduced proliferation and/or increased death.
8. **(Withdrawn)** The method of claim 5, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.
9. **(Withdrawn)** The method of claim 8, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.
10. **(Currently Amended)** The method of claim 1, wherein ~~the~~ said lung cancer cells are selected from the group consisting of lung cancer cell lines and lung cancer cells obtained from a patient.
11. **(Currently Amended)** The method of claim 1, wherein ~~the~~ said agent is a chemotherapeutic compound.
12. **(Currently Amended)** The method of claim 11, wherein ~~the~~ said agent is a platinum compound.

13. **(Currently Amended)** The method of claim 12, wherein ~~the said~~ agent is cisplatin.

14. **(Currently Amended)** A method for determining whether an agent is effective in treating lung cancer, comprising the steps of: a) obtaining a sample of lung cancer cells; b) exposing the said sample to an agent; c) determining and quantifying the level of expression of a marker genes, wherein said marker gene is comprising ABCC5, GTF2H2 and/or ERCC2, in the said sample exposed to the said agent and in a sample that is not exposed to the said agent; and d) identifying that an said agent is effective in treating cancer when expression of said marker genes is altered in the presence of said agent in said sample exposed to said agent as compared to expression of said marker gene in said sample not exposed to said agent.

15. **(Currently Amended)** The method of claim 14, wherein ~~the said level of~~ expression of said marker genes in the said sample is assessed by detecting the presence in the said sample of a transcribed polynucleotide or portion thereof, ~~wherein the transcribed polynucleotide comprises the of said marker gene.~~

16. **(Currently Amended)** The method of claim 15, wherein ~~the said~~ transcribed polynucleotide is an mRNA ~~or~~ siRNA.

17. **(Currently Amended)** ~~A~~ The method of claim 15, wherein ~~the said~~ transcribed polynucleotide is a cDNA.

18. **(Withdrawn)** The method of claim 14, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to the marker.

19. **(Currently Amended)** The method of claim 15, wherein the step of detecting further comprises amplifying the said transcribed polynucleotide using RT-PCR.

20. **(Previously presented)** The method of claim ~~19~~14, wherein ~~the step of detecting the level of expression includes:~~

~~initially screening a plurality of genes representing different functional classes,
evaluating an expanded group of genes represented by genes that are positively
associated in the initial screening,~~

~~comparing the expression of the positively or negatively associated genes said
level of expression of said marker gene is used with the level of expression of another
marker gene to form at least one interactive gene expression index (IGEI), wherein said
IGEI comprises a ratio of said level of expression of said marker gene and said level of
expression of another marker gene~~

~~using the IGEI analysis, and~~

~~developing at least one model that describes an association between the level of
detection of the expression of at least one of the markers identified in Tables 1 and 5 and
reduced proliferation and/or cell death.~~

21. *(Withdrawn)* The method of claim 19, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.

22. *(Withdrawn)* The method of claim 21, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.

23. *(Currently Amended)* The method of claim 14, wherein ~~the said lung~~ cancer cells are selected from the group consisting of lung cancer cell lines and lung cancer cells obtained from a patient.

24. *(Currently Amended)* The method of claim 14, wherein ~~the said~~ agent is a chemotherapeutic compound.

25. *(Currently Amended)* The method of claim 24, wherein ~~the said~~ agent is a platinum compound.

26. *(Currently Amended)* The method of claim ~~26~~25, wherein ~~the said~~ agent is cisplatin.

27. **(Currently Amended)** A method for determining whether treatment with an agent should be continued in a lung cancer patient, comprising the steps of: a) obtaining two or more samples comprising lung cancer cells from a patient during the course of treatment with ~~the~~said agent; b) determining and quantifying the levels of expression of a marker genes in said two or more samples, wherein said marker gene is comprising ABCC5, GTF2H2 ~~and/or ERCC2 in the two or more samples~~; and c) continuing treatment when the expression levels of ~~at least one of~~ said marker genes is not significantly altered during the course of treatment.

28. **(Currently Amended)** The method of claim 27, wherein ~~the~~said levels of expression of said marker genes in ~~the~~said sample ~~are~~is assessed by detecting the presence in ~~the~~said sample of a transcribed polynucleotide or portion thereof, ~~wherein the transcribed polynucleotide comprises the~~ of said marker gene.

29. **(Currently Amended)** The method of claim 28, wherein ~~the~~said transcribed polynucleotide is an mRNA ~~or siRNA~~.

30. **(Currently Amended)** ~~A~~The method of claim 28, wherein ~~the~~said transcribed polynucleotide is a cDNA.

31. **(Withdrawn)** The method of claim 27, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to the marker.

32. **(Currently Amended)** The method of claim 28, wherein the step of detecting further comprises amplifying ~~the~~said transcribed polynucleotide using RT-PCR.

33. **(Currently Amended)** The method of claim ~~32~~27, wherein ~~the step of detecting the level of expression includes:~~

~~initially screening a plurality of genes representing different functional classes;
evaluating an expanded group of genes represented by genes that are positively or
negatively associated in the initial screening;~~

~~comparing the expression of the positively and negatively associated genes said level of expression of said marker gene is used with the level of expression of another marker gene to form at least one interactive gene expression index (IGEI), wherein said IGEI comprises a ratio of said level of expression of said marker gene and said level of expression of another marker gene using the IGEI analysis, and developing at least one model that describes an association between the level of detection of the expression of at least one of the markers identified in Tables 1 and 5 and reduced proliferation and/or cell death.~~

34. *(Withdrawn)* The method of claim 31, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.

35. *(Withdrawn)* The method of claim 34, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.

36. *(Currently Amended)* The method of claim 27, wherein ~~the said~~ lung cancer cells are selected from the group consisting of lung cancer cell lines and lung cancer cells obtained from a patient.

37. *(Currently Amended)* The method of claim ~~2927~~, wherein ~~the said~~ agent is a chemotherapeutic compound.

38. *(Currently Amended)* The method of claim ~~3837~~, wherein ~~the said~~ agent is a platinum compound.

39. *(Currently Amended)* The method of claim 38, wherein ~~the said~~ agent is cisplatin.

40. *(Currently Amended)* A method for identifying new cancer treatments, comprising the steps of: a) obtaining a sample of lung cancer cells; b) determining and

quantifying the levels of expression of a marker genes in said sample, wherein said marker gene is comprising ABCC5, GTF2H2 and/or ERCC2; c) exposing ~~the said~~ sample to ~~the a~~ cancer treatment; d) determining ~~said the level of~~ expression levels of said marker in the said sample exposed to ~~the said~~ cancer treatment; and e) identifying that ~~the said~~ cancer treatment is effective in treating cancer when ~~at least one of~~ said marker genes is expressed at a ~~certain level~~ comparable to a previously determined level of said marker in cells with known sensitivity to a cancer agent.

41. **(Currently Amended)** The method of claim 40, wherein ~~the said~~ level of expression of ~~the said~~ marker gene in ~~the said~~ sample is assessed by detecting the presence in ~~the said~~ sample of a transcribed polynucleotide or portion thereof, ~~wherein the transcribed polynucleotide comprises the of said marker gene~~.

42. **(Currently Amended)** The method of claim 41, wherein ~~the said~~ transcribed polynucleotide is an mRNA ~~or siRNA~~.

43. **(Currently Amended)** ~~A~~ The method of claim 41, wherein ~~the said~~ transcribed polynucleotide is a cDNA.

44. **(Withdrawn)** The method of claim 40, wherein the level of expression of the marker in the sample is assessed by detecting the presence in the sample of a protein or protein fragment corresponding to the marker.

45. **(Currently Amended)** The method of claim 40~~41~~, wherein the step of detecting further comprises amplifying ~~the said~~ transcribed polynucleotide using RT-PCR.

46. **(Currently Amended)** The method of claim 45~~40~~, wherein ~~the step of detecting the level of expression includes:~~

~~initially screening a plurality of genes representing different functional classes;
evaluating an expanded group of genes represented by genes that are positively or negatively associated in the initial screening;~~

~~comparing the expression of the positively and negatively associated genes said level of expression of said marker gene is used with the level of expression of another gene to form at least one interactive gene expression index (IGEI), wherein said IGEI comprises a ratio of said level of expression of said marker gene and said level of expression of another marker gene~~

~~using the IGEI analysis, and~~

~~developing at least one model that describes an association between the level of detection of the expression of at least one of the markers identified in Tables 1 and 5 and reduced proliferation and/or cell death.~~

47. *(Withdrawn)* The method of claim 44, wherein the presence of the protein or protein fragment is detected using a reagent which specifically binds with the protein or protein fragment.

48. *(Withdrawn)* The method of claim 47, wherein the reagent is selected from the group consisting of an antibody, an antibody derivative, and an antibody fragment.

49. *(Currently Amended)* The method of claim 40, wherein ~~the said lung~~ cancer cells are selected from the group consisting of lung cancer cell lines and lung cancer cells obtained from a patient.

50. *(Currently Amended)* The method of claim 40, wherein ~~the said~~ agent is a chemotherapeutic compound.

51. *(Currently Amended)* The method of claim 50, wherein ~~the said~~ agent is a platinum compound.

52. *(Currently Amended)* The method of claim 51, wherein ~~the said~~ agent is cisplatin.

53. *(Withdrawn)* A method of diagnosing non small cell lung cancer in a patient, comprising: (a) detecting and quantifying the level of expression in a tissue sample of c myc,

E2F 1 and p21 genes; wherein differential expression of the c myc, E2F 1 and p21 genes is indicative of non small cell lung cancer.

54. *(Withdrawn)* A method of detecting the progression of non small cell lung cancer in a patient, comprising: (a) detecting and quantifying the level of expression in a tissue sample of two or more c myc, E2F 1 and p21 genes; wherein differential expression of the c myc, E2F 1 and p21 genes is indicative of non small cell lung cancer progression.

55. *(Withdrawn)* A method of monitoring the treatment of a patient with non small cell lung cancer, comprising: (a) administering a pharmaceutical composition to the patient; (b) preparing a gene expression profile from a cell or tissue sample from the patient; and (c) comparing the patient gene expression profile to a gene expression from a cell population selected from the group consisting of normal lung cells, and non small cell lung cancer.

56. *(Withdrawn)* A method of treating a patient with non small cell lung cancer, comprising: (a) administering to the patient a pharmaceutical composition, wherein the composition alters the expression of at least one gene in Tables 1 and 5 or c myc, E2F 1 and p21 genes; (b) preparing an IGEI comprising standardized gene expression values using StART PCR from a cell or tissue sample comprising tumor cells obtained before treatment and another sample obtained after treatment; and (c) comparing the sample obtained prior to treatment with the sample obtained after treatment.

57. *(Currently Amended)* A method of screening for an agent capable of modulating the onset or progression of non small cell lung cancer, comprising: (a) preparing a first IGEI comprising standardized gene expression values using StART PCR of a cell population comprising non small cell lung cancer cells, wherein thesaid first IGEI comprises ~~determines~~ the expression level of one or more genes from Tables 1 and 5 or c myc, E2F 2 and p21 genes ABCC5, GTF2H2 or ERCC2; (b) exposing thesaid cancer cells ~~population to the said~~ agent; (c) preparing a second IGEI comprising standardized gene expression values using StART PCR of thesaid agent-exposed cancer cells ~~population~~; and (d) comparing thesaid first and thesaid second IGEIs; and (e) identifying said agent as capable of modulating the onset or

progression of non small cell lung cancer when said values of said first and said second IGEIs are not significantly different.

58. **(Withdrawn)** A solid phase hybridization template for measuring, in a standardized fashion, PCR products following standardized quantitative RT PCR comprising:

- (a) preparing at least one solid phase hybridization template where, for each gene, an oligonucleotide of any length that will bind with specificity to both the competitive template, CT, and native template, NT, is spotted to a filter;
- (b) identifying a suitable oligonucleotide such that the region between the forward primer (common to both the NT and CT) and the 3' 20 bp of the reverse CT primer is evaluated;
- (c) attaching an oligonucleotide to a solid support at a previously designated location;
- (d) amplifying the CT and NT PCR products and hybridizing to the spots of the filter wherein each gene (NT and CT) are amplified separately;
- (e) pooling the PCR products for hybridization;
- (f) preparing two oligonucleotide probes, each labeled with a different fluor, for each gene wherein one oligonucleotide is homologous to, and will bind to sequences unique to the NT for a gene that was PCR-amplified such that this oligonucleotide binds to the region of the NT that is not homologous to the CT and is labeled with a different fluor, and wherein the other oligonucleotide is specific to the CT and is labeled with a different fluor such that this other oligonucleotide is homologous to and will bind to CT sequences that span the 3' end of the reverse primer.

59. **(Withdrawn)** The solid phase hybridization template of claim 58 wherein the NT specific and CT specific oligonucleotides for multiple genes are mixed in equal amounts and hybridized to the gene-specific PCR products bound to the gene-specific oligonucleotides spotted on the filter.

60. **(Withdrawn)** The solid phase hybridization template of claim 59 wherein the ratio between the fluors bound to the spot quantifies the NT relative to CT.

61. **(Withdrawn)** The solid phase hybridization template of claim 60, wherein, although there may be different binding affinities between the CT and CT probe relative to that between the NT and NT probe, this difference is consistent between different samples assessed, and from one experiment to another.

62. **(Withdrawn)** The solid phase hybridization template of claim 58 wherein the template comprises at least one standardized microarray, microbeads, glass slides, or chips prepared by photolithography.

63. **(Withdrawn)** The solid phase hybridization template of claim 60, wherein the solid support comprises at least one of a membrane, a glass support, a filter, a tissue culture dish, a polymeric material, a bead and a silica support.

64. **(Withdrawn)** The solid phase hybridization template of claim 63, wherein the solid support comprising at least two oligonucleotides, wherein each of the oligonucleotides comprises a sequence that specifically hybridizes to at least one gene in Tables I and 5 or the c-myc, E2F 1 and p21 genes.

65. **(Withdrawn)** The solid phase hybridization template of claim 64, wherein the oligonucleotides are covalently attached to the solid support.

66. **(Withdrawn)** The solid phase hybridization template of claim 64, wherein the oligonucleotides are non-covalently attached to the solid support.

67. **(Withdrawn)** A computer system comprising: (a) a database containing information identifying the standardized numerical expression level in units of molecules/106 β actin molecules in lung tissue of a set of genes comprising at least two genes in Tables 1 and 5 or c-myc, E2F 1 and p21 genes; and (b) a user interface to view the information.

68. **(Withdrawn)** A computer system of claim 67, wherein the database further comprises sequence information for the genes.

69. **(Withdrawn)** A computer system of claim 67, wherein the database further comprises information identifying the standardized numerical expression level in units of molecules/ 10^6 β actin molecules for the set of genes in normal lung tissue.

70. **(Withdrawn)** A computer system of claim 67, wherein the database further comprises information identifying the standardized numerical expression level in units of molecules/ 10^6 β actin molecules of the set of genes in non small cell cancer tissue.

71. **(Withdrawn)** A computer system of any of claims 67-70, further comprising records including descriptive information from an external database, which information correlates said genes to records in the external database.

72. **(Withdrawn)** A computer system of claim 71, wherein the external database is Genbank.

73. **(Withdrawn)** A method of using a computer system of any one of claims 67-72 to present information identifying the standardized numerical expression level in a tissue or cell of at least one gene in Tables 1 and 5 and c myc, E2F 1 and p21 genes, comprising: (a) comparing the standardized numerical expression level of at least one gene in Tables 1 and 5 or c myc, E2F 1 and p21 genes in the tissue or cell to the level of expression of the gene in the database.

74. **(Withdrawn)** A method of claim 73, wherein the expression level of at least two genes are compared.

75. **(Withdrawn)** A method of claim 73, wherein the expression level of at least five genes are compared.

76. **(Withdrawn)** A method of claim 73, wherein the expression level of at least ten genes are compared.

77. **(Withdrawn)** A method of claim 73, further comprising displaying the level of expression of at least one gene in the tissue or cell sample compared to the expression level in lung cancer or in normal lung tissue.

78. **(Withdrawn)** A kit comprising at least one solid support of any one of claims 64-66 packaged with gene expression information for said genes.

79. **(Withdrawn)** A kit of claim 78, wherein the gene expression information comprises gene expression levels in a tissue or cell sample exposed to a toxin.

80. **(Withdrawn)** A kit of claim 79, wherein the gene expression information is in an electronic format.

81. **(Withdrawn)** The method of claims 1, 14, 27 or 40, wherein said marker genes further comprise ERCC3, LIG1, ACTB, XPC, ABCC1, ABCC4, ABCC10, XRCC1, XPA, XPC, XRCC1 and DDIT3.

82. **(Currently Amended)** A method for determining whether an agent can be used to reduce the proliferation, inhibit the growth, and/or cause the death of lung cancer cells or inhibit the growth of a cancer cell population, comprising the steps of: a) obtaining a sample of lung cancer cells; b) determining and quantifying the level of expression of at least two marker genes in the said lung cancer cells of, wherein said at least two marker genes are ERCC2, ERCC3, LIG1, ACTB, XPC, ABCC1, ABCC4, ABCC5, ABCC10, or GTF2H2, XRCC1, XPA, XPC, XRCC1, DDIT3 or a combination thereof; and c) identifying that an agent can be used to reduce the proliferation, inhibit the growth, and/or cause the death of said lung cancer cells when said two or more markers are expressed at a certain level comparable to a previously determined level of said marker genes in cells with known sensitivity to said agent.

83. *(Withdrawn)* The method of claim 82, wherein said determining and quantifying is of ABCC5 and GTF2H2 genes.

84. *(Withdrawn)* The method of claim 82, wherein said determining and quantifying is of ERCC2 and GTF2H2 genes.

85. *(Withdrawn)* The method of claim 82, wherein said determining and quantifying is of ERCC2 and XPC genes.

86. *(Withdrawn)* The method of claim 82, wherein said determining and quantifying is of ERCC2 and XRCC1 genes.

87. *(Withdrawn)* The method of claim 82, wherein said determining and quantifying is of XPA and XPC genes.

88. *(Withdrawn)* The method of claim 82, wherein said determining and quantifying is of XRCC1 and XPC genes.

89. *(Withdrawn)* The method of claim 82, wherein said determining and quantifying is of ABCC5 and XPC genes.

90. *(New)* A method of identifying a marker for determining the sensitivity of a lung cancer cell to an agent effective in reducing proliferation, inhibiting growth, or promoting cell death of a lung cancer cell comprising: (a) screening a plurality of genes representing different functional classes; (b) identifying genes from step (a) that are correlated to sensitivity to said agent; (c) evaluating an expanded group of genes, wherein said expanded group of genes are genes in the same functional class as genes identified in (b); (d) using the expression data of genes identified in step (b) and said expanded group of genes in step (c) to form interactive gene expression indices (IGEIs); and, (e) using said IGEIs to develop at least one model that describes an association between expression of at least one gene and sensitivity of said cancer cell to said agent.